

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

CLAIMS

Claims 1-16. **(Cancelled)**

17. **(Original)** A method for preventing and/or treating urinary tract disease, which comprises administering an effective amount of a medicament comprising a combination of EP₁ antagonist and EP₃ antagonist to a mammal.

18. **(Currently Amended)** ~~A The method according to claim 17 for preventing and/or treating urinary tract disease, which comprises administering an effective amount of a compound having antagonism to wherein the EP₁ antagonist and antagonism to the EP₃ antagonist is the same compound to a mammal.~~

Claims 19-20. **(Cancelled)**

21. **(New)** The method according to claim 17, wherein the urinary tract disease is lower urinary tract disorder.

22. **(New)** The method according to claim 17, wherein the urinary tract disease is urinary storage disorder.

23. **(New)** The method according to claim 22, wherein the urinary storage disorder is overactive bladder.

24. **(New)** The method according to claim 23, wherein the overactive bladder is urgency of urination, bladder pain or urine incontinence.

25. (New) The method according to claim 23, wherein the overactive bladder is frequent urination.

26. (New) The method according to claim 24, wherein the urine incontinence is urgency incontinence, stress urinary incontinence, overflow incontinence, psychogenic incontinence or complex incontinence.

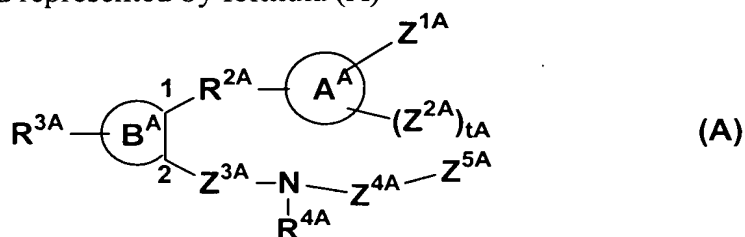
27. **(New)** The method according to claim 17, wherein the medicament is useful for improving urine retaining ability.

28. (New) The method according to claim 17, wherein the medicament is useful for improving bladder compliance.

29. **(New)** The method according to claim 17, wherein the medicament is useful for relieving hypertonic detrusor muscle.

30. **(New)** The method according to claim 17, wherein the EP₁ antagonist is a compound selected from a group consisting of

a compound represented by formula (A)



wherein $\textcircled{\text{A}^{\text{A}}}$ and $\textcircled{\text{B}^{\text{A}}}$ are each independently C5-15 carbocyclic ring or 5- to 7-

membered heterocyclic ring having 1 or 2 oxygen, sulfur or nitrogen atoms;

Z^{1A} is a group represented by -COR^{1A}, -C1-4 alkylene-COR^{1A}, -CH=CH-COR^{1A}, -C≡C-COR^{1A}, -O-C1-3 alkylene-COR^{1A} wherein R^{1A} is hydroxy, C1-4 alkoxy or a group represented

by formula $\text{NR}^{6\text{A}}\text{R}^{7\text{A}}$ wherein $\text{R}^{6\text{A}}$ and $\text{R}^{7\text{A}}$ are independently hydrogen atom or C1-4 alkyl or -C1-5 alkylene-OH;

$\text{Z}^{2\text{A}}$ is a hydrogen atom, C1-4 alkyl, C1-4 alkoxy, nitro, halogen, trifluoromethyl, trifluoromethoxy, hydroxy or a group represented by formula $\text{COR}^{1\text{A}}$ wherein $\text{R}^{1\text{A}}$ has the same meaning as described above;

$\text{Z}^{3\text{A}}$ is a single bond or C1-4 alkylene;

$\text{Z}^{4\text{A}}$ is SO_2 or CO;

$\text{Z}^{5\text{A}}$ is (1) C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, (2) phenyl, C3-7 cycloalkyl, 5- to 7-membered heterocyclic ring having 1 or 2 oxygen, sulfur or nitrogen atoms, (3) C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl substituted by phenyl or C3-7 cycloalkyl wherein phenyl, C3-7 cycloalkyl and 5- to 7-membered heterocyclic ring having 1 or 2 oxygen, sulfur or nitrogen atoms in above-described (2) and (3) may be substituted by 1 to 5 $\text{R}^{5\text{A}}$ groups wherein multiple $\text{R}^{5\text{A}}$'s are independently a hydrogen atom, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, nitro, halogen, trifluoromethyl, trifluoromethoxy or hydroxy;

$\text{R}^{2\text{A}}$ is $\text{CONR}^{8\text{A}}$, $\text{NR}^{8\text{A}}\text{CO}$, $\text{CONR}^{8\text{A}}\text{-C1-4 alkylene}$, $\text{C1-4 alkylene-CONR}^{8\text{A}}$, $\text{NR}^{8\text{A}}\text{CO-C1-4 alkylene}$, $\text{C1-4 alkylene-NR}^{8\text{A}}\text{CO}$, $\text{C1-3 alkylene-CONR}^{8\text{A}}\text{-C1-3 alkylene}$, $\text{C1-3 alkylene-NR}^{8\text{A}}\text{CO-C1-3 alkylene}$ wherein $\text{R}^{8\text{A}}$ is a hydrogen atom or C1-4 alkyl, O, S, $\text{NZ}^{6\text{A}}$ wherein $\text{Z}^{6\text{A}}$ is a hydrogen atom or C1-4 alkyl, $\text{Z}^{7\text{A}}\text{-C1-4 alkylene}$, $\text{C1-4 alkylene-Z}^{7\text{A}}$, $\text{C1-3 alkylene-Z}^{7\text{A}}\text{-C1-3 alkylene}$ wherein $\text{Z}^{7\text{A}}$ is O, S or $\text{NZ}^{6\text{A}}$ wherein $\text{Z}^{6\text{A}}$ has the same meaning as described above, CO, CO-C1-4 alkylene, C1-4 alkylene-CO, C1-3 alkylene-CO-C1-3 alkylene, C2-4 alkylene, C2-4 alkenylene or C2-4 alkynylene;

$\text{R}^{3\text{A}}$ is a hydrogen atom, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, nitro, halogen, trifluoromethyl, trifluoromethoxy, hydroxy or hydroxymethyl;

$\text{R}^{4\text{A}}$ is (1) a hydrogen atom, (2) C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, (3) C1-6 alkyl substituted by 1 or 2 group(s) selected from $\text{COOZ}^{8\text{A}}$, $\text{CONZ}^{9\text{A}}\text{Z}^{10\text{A}}$, $\text{OZ}^{8\text{A}}$ wherein $\text{Z}^{8\text{A}}$, $\text{Z}^{9\text{A}}$ and

Z^{10A} are independently a hydrogen atom or C1-4 alkyl, C1-4 alkoxy-C1-4 alkoxy, (4) C3-7 cycloalkyl, (5) C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl substituted by phenyl or C3-7 cycloalkyl wherein phenyl or C3-7 cycloalkyl in above-described (4) and (5) may be substituted by 1 to 5 R^{5A} groups wherein R^{5A} has the same meaning as described above; n^A and t^A are each independently an integer from 1 to 4, and

wherein

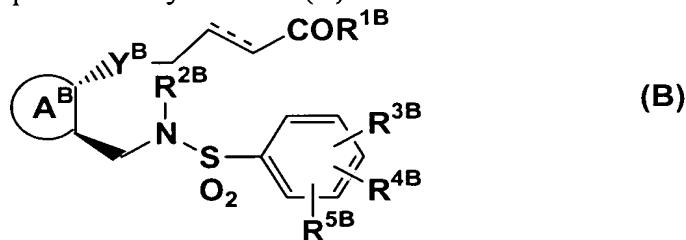
(1) R^{2A} and Z^{3A} are each connected at the 1- or 2-position of $\textcircled{B^A}$; and

(2) when $\textcircled{A^A}$ is benzene and $(Z^{2A})_{tA}$ is other than COR^{1A} , Z^{1A} is connected at the 3-

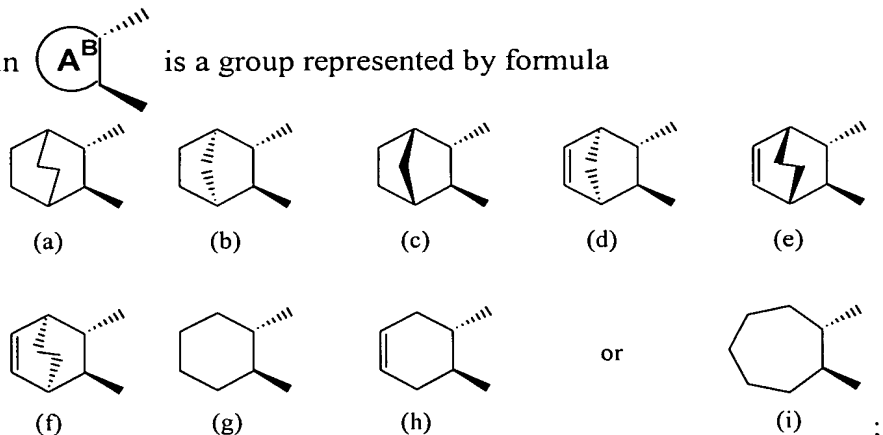
or 4-position of benzene,

a salt thereof, a solvate thereof or a prodrug thereof,

a compound represented by formula (B)



wherein $\textcircled{A^B}$ is a group represented by formula




R^{1B} is hydroxy, C1-4 alkoxy or a group represented by formula $NR^{6B}R^{7B}$ wherein R^{6B} and R^{7B} are each independently a hydrogen atom or C1-4 alkyl;

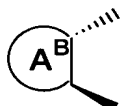
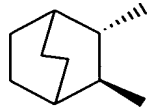
R^{2B} is a hydrogen atom or C1-4 alkyl;


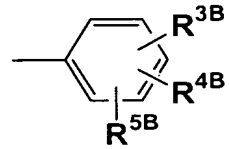
R^{3B} and R^{4B} are each C1-4 alkyl, a halogen atom or trifluoromethyl;

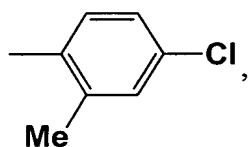
R^{5B} is a hydrogen atom, C1-4 alkyl, a halogen atom or trifluoromethyl;

Y^B is cis-vinylene or trans-vinylene;

symbol  is a single bond or double bond, and

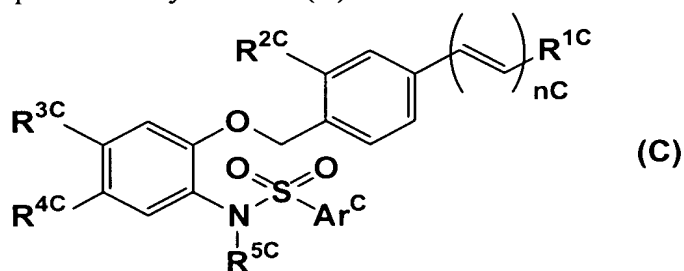
wherein, when  is formula , R^{1B} is hydroxy or C1-4 alkoxy, R^{2B} is

a hydrogen atom, Y^B is cis-vinylene and symbol  is a single bond,  is not



a salt thereof, a solvate thereof or a prodrug thereof, and

a compound represented by formula (C)



wherein R^{1C} is $COOH$, 5-tetrazolyl, 5-oxo-1,2,4-oxadiazolyl, CH_2OH or 5-oxo-1,2,4-thiadiazolyl;

R^{2C} is hydrogen, methyl, methoxy or chloro;

R^{3C} and R^{4C} are a combination of (1) methyl and methyl, (2) methyl and chloro, (3) chloro and methyl or (4) trifluoromethyl and hydrogen, or are taken together with the carbon atom to which they are attached to form (5) cyclopentene, (6) cyclohexene or (7) benzene;

R^{5C} is isopropyl, isobutyl, 2-methyl-2-propenyl, cyclopropylmethyl, methyl, ethyl, propyl, 2-propenyl or 2-hydroxy-2-methylpropyl;

Ar^C is thiazolyl which may be substituted by methyl, pyridyl or 5-methyl-2-furyl;

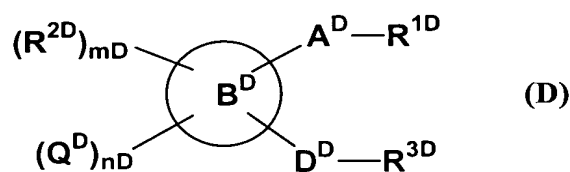
n^C is 0 or 1, and

wherein, when R^{1C} is 5-tetrazolyl, 5-oxo-1,2,4-oxadiazolyl or 5-oxo-1,2,4-thiadiazolyl, n^C is 0,
an alkyl ester thereof, a salt thereof or a prodrug thereof.

31. **(New)** The method according to claim 30, wherein the compound is
4-[6-[N-isobutyl-N-(4-methyl-2-thiazolylsulfonyl)amino]indan-5-yloxymethyl]benzoic acid or
3-methyl-4-[6-[N-isobutyl-N-(4-methyl-2-thiazolylsulfonyl)]amino]indan-5-yloxymethyl]cinnamic acid.

32. **(New)** The method according to claim 17, wherein the EP₃ antagonist is a compound selected from a group consisting of

a compound represented by formula (D)



wherein R^{1D} is $-COOH$, $-COOR^{4D}$, $-CH_2OH$, $-CONR^{5D}SO_2R^{6D}$, $-CONR^{7D}R^{8D}$, $-CH_2NR^{5D}SO_2R^{6D}$, $-CH_2NR^{9D}COR^{10D}$, $-CH_2NR^{9D}CONR^{5D}SO_2R^{6D}$, $-CH_2SO_2NR^{9D}COR^{10D}$, $-CH_2OCONR^{5D}SO_2R^{6D}$, tetrazole, 1,2,4-oxadiazol-5-one, 1,2,4-oxadiazole-5-thione, 1,2,4-thiadiazol-5-one, 1,3-thiazolidine-2,4-dione, or 1,2,3,5-oxathiadiazol-2-one;

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R^{4D} is C1-6 alkyl or (C1-4 alkylene)- R^{11D} ;

R^{11D} is hydroxy, C1-4 alkoxy, -COOH, C1-4 alkoxycarbonyl or -CONR^{7D}R^{8D};

R^{5D} is a hydrogen atom or C1-6 alkyl;

R^{6D} is

- (i) C1-6 alkyl,
- (ii) C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{12D} groups or unsubstituted, or
- (iii) C1-6 alkyl, C2-6 alkenyl or C2-6 alkynyl substituted by C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{12D} groups or unsubstituted;

R^{7D} and R^{8D} are each independently

- (i) a hydrogen atom,
- (ii) C1-6 alkyl,
- (iii) hydroxy,
- (iv) -COR^{17D},
- (v) C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{12D} groups or unsubstituted, or
- (vi) C1-4 alkyl substituted by C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{12D} groups or unsubstituted;

R^{9D} is a hydrogen atom or C1-6 alkyl;

R^{10D} is

- (i) a hydrogen atom,
- (ii) C1-6 alkyl,
- (iii) C3-15 mono-, bi- or tri-carbocyclic ring or 3-15 membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{12D} groups or unsubstituted, or

(iv) C1-6 alkyl, C2-6 alkenyl or C2-6 alkynyl substituted with C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{12D} groups or unsubstituted;

R^{12D} is (a) C1-6 alkyl, (b) C1-6 alkoxy, (c) C1-6 alkylthio, (d) a halogen atom, (e) CF_3 , (f) cyano, (g) nitro, (h) hydroxy, (i) $-COOR^{13D}$, (j) $-NHCOR^{13D}$, (k) $-SO_2R^{14D}$, (l) $-NR^{15D}R^{16D}$, (m) C3-7 mono-carbocyclic ring substituted by C1-4 alkyl or oxo or unsubstituted, (n) 3- to 7-membered mono-heterocyclic ring substituted by C1-4 alkyl or oxo or unsubstituted or (o) C1-4 alkyl substituted by hydroxy, $-COOR^{13D}$, $-NHCOR^{13D}$, $-SO_2R^{14D}$, or $-NR^{15D}R^{16D}$;

R^{13D} is a hydrogen atom, C1-4 alkyl, phenyl, or phenyl(C1-4)alkyl;

R^{14D} is C1-4 alkyl;

R^{15D} and R^{16D} are each independently a hydrogen atom, C1-4 alkyl, phenyl, phenyl(C1-4)alkyl;

R^{17D} is C1-4 alkyl or phenyl;

A^D is

- (i) a single bond,
- (ii) C1-6 alkylene,
- (iii) C2-6 alkenylene,
- (iv) C2-6 alkynylene,
- (v) $-O-(C1-3 \text{ alkylene})$,
- (vi) $-S-(C1-3 \text{ alkylene})$,
- (vii) $-NR^{20D}-(C1-3 \text{ alkylene})$,
- (viii) $-CONR^{21D}-(C1-3 \text{ alkylene})$,
- (ix) $-(C1-3 \text{ alkylene})-O-(C1-3 \text{ alkylene})$,
- (x) $-(C1-3 \text{ alkylene})-S-(C1-3 \text{ alkylene})$,
- (xi) $-(C1-3 \text{ alkylene})-NR^{20D}-(C1-3 \text{ alkylene})$,

- (xii) $-(C1-3 \text{ alkylene})-CONR^{21D}-(C1-3 \text{ alkylene})$,
- (xiii) $-Cyc1^D$,
- (xiv) $-(C1-4 \text{ alkylene})-Cyc1^D$, or
- (xv) $-Cyc1^D-(C1-4 \text{ alkylene})$,

wherein the alkylene, alkenylene and alkynylene in A^D may be substituted by 1 to 6 substituents selected from the following substituents of (a)-(i):

(a) C1-6 alkyl, (b) C1-6 alkoxy, (c) halogen atom, (d) CHF_2 , (e) CF_3 , (f) $OCHF_2$, (g) OCF_3 , (h) hydroxy, (i) hydroxy(C1-4) alkyl;

R^{20D} is a hydrogen atom, C1-4 alkyl, $-SO_2(C1-4)alkyl$ or C2-5 acyl;

R^{21D} is a hydrogen atom or C1-4 alkyl;

$Cyc1^D$ is C3-7 mono-carbocyclic ring or 3- to 7-membered mono-heterocyclic ring substituted with 1 to 4 substituents selected from C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halogen atom, CHF_2 , CF_3 , nitro and cyano or unsubstituted;

B^D ring is C3-12 mono- or bi-carbocyclic ring or 3- to 12-membered mono- or bi-heterocyclic ring;

R^{2D} is C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halogen atom, CHF_2 , CF_3 , nitro, cyano, phenyl or oxo;

m^D is 0, 1 or 2,

wherein

when $-D-R^{3D}$ binds to B^D ring at the ortho position based on $-A^D-R^{1D}$, then n^D is 1 or 2,

and

when $-D-R^{3D}$ binds to B^D ring at the non-ortho position based on $-A^D-R^{1D}$, then n^D is 0, 1 or 2;

Q^D is

- (1) (i) $-(C1-4 \text{ alkylene}, C2-4 \text{ alkenylene or } C2-4 \text{ alkynylene})-Cyc2^D$,

- (ii) $-(C1-4 \text{ alkylene})-Z^D-Cyc3^D$,
 - (iii) C1-4 alkyl substituted by substituent(s) selected from $-NR^{24D}R^{25D}$, $-S(O)_{pD}R^{26D}$, cyano, $-NR^{23D}COR^{27D}$, $-NR^{23D}SO_2R^{28D}$ and $-NR^{23D}CONR^{24D}R^{25D}$
 - (iv) a group selected from C1-4 alkoxy(C1-4)alkoxy, $-NR^{23D}COR^{27D}$, $-COR^{28D}$, $-OSO_2R^{28D}$, $-NR^{23D}SO_2R^{28D}$ and $-NR^{23D}CONR^{24D}R^{25D}$,
 - (v) C3-7 mono-carbocyclic ring or 3- to 6-membered mono-heterocyclic ring substituted with 1 to 5 R^{30D} 's, wherein one of the R^{30D} 's binds to the ring at the non 1-position,
 - (vi) C8-15 mono-, bi- or tri-carbocyclic ring or 7- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted,
 - (vii) $-T^D-Cyc5^D$ or
 - (viii) a group selected from $-L^D-Cyc6-1^D$, $-L^D-(C3-6 \text{ cycloalkyl})$, $-L^D-CH_2-(C3-6 \text{ cycloalkyl})$, $-L^D-(C2-4 \text{ alkylene})-Cyc6^D-2$ and $-L^D-(C1-4 \text{ alkylene})_{qD}-Cyc6^D-3$ wherein the C3-6 cycloalkyl is substituted by 1 to 5 R^{30D} 's or unsubstituted,
- (2) (i) phenoxy,
- (ii) benzyloxy,
 - (iii) hydroxy(C1-4)alkyl,
 - (iv) C1-4 alkoxy(C1-4)alkyl or
 - (v) $-(C1-4 \text{ alkylene})-O\text{-benzyl}$, or
- (3) (i) C2-6 alkenyl,
- (ii) C2-6 alkynyl,
 - (iii) C1-6 alkyl substituted by 1 to 3 halogen atoms,
 - (iv) cyano,
 - (v) nitro,
 - (vi) $-NR^{33D}R^{34D}$,
 - (vii) $-CONR^{33D}R^{34D}$,

(viii) $-S(O)_{pD}-(C1-4)alkynyl$,

(ix) $-S(O)_{pD}-CHF_2$,

(x) $-S(O)_{pD}-NR^{33D}R^{34D}$,

(xi) $-O-(C3-6)alkynyl$,

(xii) $-O-CHF_2$, or

(xiii) C3-7 cycloalkyl;

R^{22D} is a hydrogen atom, C1-4 alkyl, $-SO_2-(C1-4)alkyl$ or C2-5 acyl;

R^{23D} is a hydrogen atom, C1-4 alkyl, phenyl or phenyl(C1-4)alkyl;

R^{24D} and R^{25D} are each independently a hydrogen atom, C1-4 alkyl, $Cyc4^D$ or (C1-4 alkylene)- $Cyc4^D$;

R^{26D} is C1-4 alkyl or $Cyc4^D$;

R^{27D} is a hydrogen atom, C1-4 alkyl, $-OR^{29D}$ or $Cyc4^D$;

R^{28D} is C1-4 alkyl, $Cyc4^D$ or $-(C1-4 alkylene)-Cyc4^D$;

R^{29D} is a hydrogen atom, C1-4 alkyl, $Cyc4^D$ or $(C1-4 alkylene)-Cyc4^D$;

R^{30D} is C1-8 alkyl, C1-8 alkoxy, C1-8 alkylthio, a halogen atom, CF_3 , OCF_3 , SCF_3 , CHF_2 , $OCHF_2$, $SCHF_2$, hydroxy, cyano, nitro, $-NR^{31D}R^{32D}$, $-CONR^{31D}R^{32D}$, formyl, C2-5 acyl, hydroxy(C1-4)alkyl, C1-4 alkoxy(C1-4)alkyl, C1-4 alkylthio(C1-4)alkyl, $-(C1-4 alkylene)-CONR^{31D}R^{32D}$, $-SO_2(C1-4)alkyl$, $-NR^{23D}CO-(C1-4)alkyl$, $-NR^{23D}SO_2-(C1-4)alkyl$, benzoyl, oxo, C3-7 mono-carbocyclic ring, 3- to 7-membered mono-heterocyclic ring, $-(C1-4 alkylene)-NR^{31D}R^{32D}$, $-M^D-(C3-7 mono-carbocyclic ring)$ or $-M^D-(3- to 7-membered mono-heterocyclic ring)$,

wherein the C3-7 mono-carbocyclic ring and 3- to 7-membered mono-heterocyclic ring in R^{30D} may be substituted with 1 to 5 substituents selected from the following (a)-(l):

(a) C1-6 alkyl, (b) C2-6 alkenyl, (c) C2-6 alkynyl, (d) C1-6 alkoxy, (e) C1-6 alkylthio, (f) halogen atom, (g) CHF_2 , (h) CF_3 , (i) nitro, (j) cyano, (k) hydroxy, (l) amino;

M^D is -O-, -S-, C1-4 alkylene, -O-(C1-4 alkylene)-, -S-(C1-4 alkylene)-, -(C1-4 alkylene)-O-, or -(C1-4 alkylene)-S-;

R^{31D} and R^{32D} are each independently a hydrogen atom or C1-4 alkyl;

$Cyc2^D$ is C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted;

Z^D is -O-, -S(O)_{pD}-, -NR^{22D}-, -NR^{23D}CO-, -NR^{23D}SO₂-, -NR^{22D}-(C1-4 alkylene)-, -S(O)_{pD}-(C1-4 alkylene)-, -O-(C2-4 alkylene)-, -NR^{23D}CO-(C1-4 alkylene) or -NR^{23D}SO₂-(C1-4 alkylene);

p^D is 0, 1 or 2;

$Cyc3^D$ is C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted;

$Cyc4^D$ is C3-12 mono- or bi-carbocyclic ring or 3- to 12-membered mono- or bi-heterocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted;

T^D is -O-, -NR^{22D}-, -O-(C1-4 alkylene)-, -S(O)_{pD}-(C1-4 alkylene)- or -NR^{22D}-(C1-4 alkylene);

$Cyc5^D$ is 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted;

q^D is 0 or 1;

L^D is -O- or -NR^{23D}-;

$Cyc6-1^D$ is phenyl or benzyl substituted by one or more R^{30D} 's;

$Cyc6-2^D$ is C3-6 mono-carbocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted;

$Cyc6-3^D$ is C7-15 mono-, bi- or tri-carbocyclic ring substituted by 1 to 5 R^{30D} 's or unsubstituted;

R^{33D} and R^{34D} are each independently a hydrogen atom, C1-4 alkyl, phenyl or benzyl, or

$\text{NR}^{3\text{D}}\text{R}^{34\text{D}}$ representing 3- to 6-membered mono-heterocyclic ring which may contain one nitrogen atom and optional one hetero atom selected from nitrogen, oxygen and sulfur atom;

D^{D} is

- (1) 1- or 2-membered linker comprising atom(s) selected from carbon, nitrogen, oxygen and sulfur atom, which may contain a double bond or a triple bond and may be substituted by 1 to 4 $\text{R}^{40\text{D}}$'s,
- (2) 3- to 6-membered linker comprising atoms selected from carbon, nitrogen, oxygen and sulfur, which may contain double bond(s) or triple bond(s) and may be substituted by 1 to 12 $\text{R}^{40\text{D}}$'s, wherein $\text{R}^{40\text{D}}$ substituted on the atom bound to $\text{R}^{3\text{D}}$, and $\text{R}^{42\text{D}}$ which is a substituent of $\text{R}^{3\text{D}}$ may be taken together to form $-(\text{CH}_2)_{y\text{D}}-$ wherein y^{D} is 1 to 4, or
- (3) 7- to 10-membered linker comprising atoms selected from carbon, nitrogen, oxygen and sulfur atom, which may contain double bonds or triple bonds and may be substituted by 1 to 20 $\text{R}^{40\text{D}}$'s, wherein $\text{R}^{40\text{D}}$ substituted on the atom binding to $\text{R}^{3\text{D}}$, and $\text{R}^{42\text{D}}$ which is a substituent of $\text{R}^{3\text{D}}$ may be taken together to form $-(\text{CH}_2)_{y\text{D}}-$;

$\text{R}^{40\text{D}}$ is (a) C1-8 alkyl, (b) C2-8 alkenyl, (c) C2-8 alkynyl, (d) oxo, (e) halogen atom, (f) CF_3 , (g) hydroxy, (h) C1-6 alkoxy, (i) C2-6 alkenyloxy, (j) C2-6 alkynyloxy, (k) OCF_3 , (l) $-\text{S}(\text{O})_{p\text{D}}-(\text{C1-6})\text{alkyl}$, (m) $-\text{S}(\text{O})_{p\text{D}}-(\text{C2-6})\text{alkenyl}$, (n) $-\text{S}(\text{O})_{p\text{D}}-(\text{C2-6})\text{alkynyl}$, (o) C2-5 acyl, (p) Cyc9^{D} , (q) C1-4 alkoxy(C1-4)alkoxy, (r) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted by 1 or 2 substituents selected from halogen atom, CF_3 , OCF_3 , hydroxy, cyano, C1-4 alkoxy, $-\text{S}(\text{O})_{p\text{D}}-(\text{C1-6})\text{alkyl}$, Cyc9^{D} and C1-4 alkoxy(C1-4)alkoxy, or

two $\text{R}^{40\text{D}}$'s may be taken together with the atom of a linker to which they bind to form C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring containing 1 to 2 hetero atoms selected from O, S, SO_2 and N, wherein the carbocyclic ring and the heterocyclic ring may be substituted by 1 to 3 substituents selected from C1-4 alkyl, C1-4 alkoxy, C2-5 acyl, $\text{SO}_2(\text{C1-4 alkyl})$, phenyl and phenyl(C1-4) alkyl;

Cyc9^D is C3-6 mono-carbocyclic ring or 3- to 6-membered mono-heterocyclic ring substituted by 1 to 5 R^{41D}'s or unsubstituted;

R^{41D} is C1-4 alkyl, C1-4 alkoxy, C1-4 alkylthio, C1-4 alkoxy(C1-4)alkyl, a halogen atom, CF₃, OCF₃, SCF₃, hydroxy, cyano, formyl, C2-5 acyl, -SO₂-(C1-4)alkyl, -NR^{23D}CO-(C1-4)alkyl, benzyl or oxo;

R^{3D} is

- (1) C1-6 alkyl or
- (2) C3-15 mono-, bi- or tri-carbocyclic ring or 3- to 15-membered mono-, bi- or tri-heterocyclic ring substituted by 1 to 5 R^{42D}'s or unsubstituted;

R^{42D} is (a) C1-6 alkyl, (b) C1-6 alkoxy, (c) C1-6 alkylthio, (d) a halogen atom, (e) cyano, (f) CF₃, (g) CHF₂, (h) OCF₃, (i) OCHF₂, (j) SCF₃, (k) -NR^{43D}R^{44D}, (l) -SO₂R^{45D}, (m) -NR^{46D}COR^{47D}, (n) hydroxy, (o) oxo, (p) C1-4 alkoxy(C1-4)alkyl, (q) Cyc10^D, (r) C1-6 alkylene-Cyc10^D, (s) -CO-Cyc10^D, (t) -W^D-Cyc10^D, (u) -(C1-6 alkylene)-W^D-Cyc10^D, (v) -W^D-(C1-6 alkylene)-Cyc10^D or (w) -(C1-6 alkylene)-W^D-(C1-6 alkylene)-Cyc10^D;

R^{43D} and R^{44D} are each independently a hydrogen atom or C1-4 alkyl;

R^{45D} is C1-4 alkyl;

R^{46D} is a hydrogen atom or C1-4 alkyl;

R^{47D} is a hydrogen atom or C1-4 alkyl;

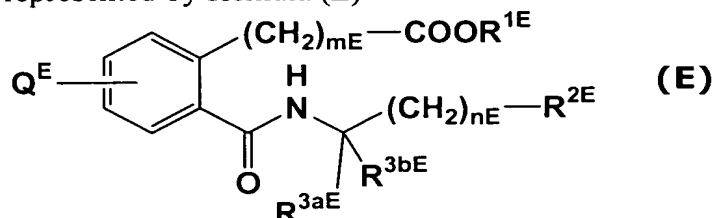
Cyc10^D is C3-12 mono- or bi-carbocyclic ring or 3- to 12-membered mono- or bi-heterocyclic ring substituted by 1 to 5 substituents selected from the following (a)-(j) or unsubstituted:

- (a) C1-4 alkyl, (b) C2-5 acyl, (c) C1-4 alkoxy, (d) a halogen atom, (e) hydroxy, (f) nitro, (g) cyano, (h) amine, (i) CF₃, (j) OCF₃;

W^D is -O-, -S(O)_{pD}- or -NR^{48D}-;

R^{48D} is a hydrogen atom or C1-4 alkyl, a salt thereof, a solvate thereof or a prodrug thereof, and

a compound represented by formula (E)



wherein R^{1E} is a hydrogen atom or C1-4 alkyl;

R^{2E} is phenyl, naphthyl, benzofuranyl or benzothienyl substituted by 1 or 2 substituents selected from C1-4 alkyl or a halogen atom or unsubstituted;

Q^E is (i) $-CH_2-O-Cyc1^E$, (ii) $-CH_2-Cyc2^E$ or (iii) $-L-Cyc3^E$;

$Cyc1^E$ is phenyl or pyridyl substituted by one or two R^{4E} 's or unsubstituted;

$Cyc2^E$ is indolyl substituted by one or two R^{4E} 's or unsubstituted;

$Cyc3^E$ is phenyl substituted by one or two R^{4E} 's or unsubstituted;

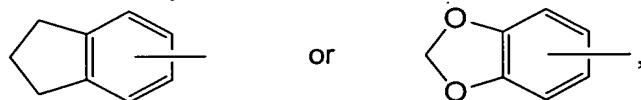
L is $-O-$ or $-NH-$;

R^{3aE} and R^{3bE} are each independently a hydrogen atom or C1-4 alkyl, or are taken together with the carbon atom to which R^{3aE} and R^{3bE} are attached to form tetrahydro-2H-pyran;

mE is 2 or 3;

nE is 0, 1 or 2;

R^{4E} is C1-4 alkyl, C1-4 alkylthio, a halogen atom or cyano, or when $Cyc3^E$ is phenyl substituted by two R^{4E} 's, and two R^{4E} 's, together with phenyl, may form



a salt thereof, a solvate thereof or a prodrug thereof.

33. (New) The method according to claim 32, wherein the compound is

N-(3,4-difluorophenylsulfonyl)-3-(2-(2-(naphthalen-2-yl)ethoxy)-4-(3-cyanophenoxymethyl)phenyl)propanamide,

3-[4-[(2,5-dimethylphenoxy)methyl]-2-({[(1R)-1-(3,5-diethylphenyl)-3-methylbutyl]amino}carbonyl)phenyl]propanoic acid,

3-(2-(((1R)-3-methyl-1-(3,5-dimethylphenyl)butyl)carbamoyl)-4-(2,5-difluorophenoxymethyl)phenyl)propanoic acid, or

3-(2-((((1R)-1-(3,5-dimethylphenyl)-3-methylbutyl)amino)carbonyl)-4-(5-fluoro-2-methylphenoxymethyl)phenyl)propanoic acid.

34. (New) The method according to claim 17, wherein the EP₁ antagonist and the EP₃ antagonist are used at low doses.